

Appl. No. 09/599,624

Atty. Docket No. 8135&

Amtd. dated October 14, 2003

Reply to Office Action of April 11, 2003

#### REMARKS

Claims 1-54 are pending in the present application. Claims 31-35, 39-41 and 48-51 have been withdrawn from consideration, in view of a previous Restriction Requirement for which the Applicants provisionally elected, with traverse, an invention and species. Further, Claims 1-30, 36-38, 42-47 and 52-54 stand as rejected.

With regard to the 35 U.S.C. 112, first paragraph, rejection of Claims 15 and 16, Applicants have amended Claims 15 and 16 to provide antecedent basis for a strong chelating agent.

New Claim 55 has been added to cover an embodiment of the present invention. No new matter has been added. Support for new Claim 55 can be found in Applicants' specification and claims as originally filed. Specifically, Claim 55 is directed to a topical composition for treating microbes, in order to inhibit or prevent the growth on the skin or scalp of said microbes, consisting essentially of: from about 0.001% to about 10%, by weight of the composition, of an anti-microbial active selected from the group consisting of polyvalent metal salts of pyrrithione; b) from about 0.001% to about 10%, by weight of the composition, of a metal ion source selected from group consisting of zinc salts, copper salts, silver salts, nickel salts, cadmium salts, mercury salts, bismuth salts, and mixtures thereof; and c) a topical carrier for the anti-microbial active and the metal salt; wherein the weight ratio of the metal source to the anti-microbial active is from about 5:100 to about 5:1 and wherein at least 50% of the anti-microbial active is insoluble in the composition.

New Claims 56 and 57 have been added to the application to cover embodiments of the present invention. No new matter has been added. Support for new Claims 56 and 57 can be found in Applicants' specification and claims as originally filed.

With regard to the 35 U.S.C. 112, first paragraph, rejection of Claim 52, Applicants would like to further direct the Examiner's attention to the support for Claim 52 found in Applicants' specification at Pages 60-63, wherein Examples 14-26 are free of from about 1 ppm to about 30 ppm of a preservative selected from the group consisting of 5-chloro-2-alkyl-4-isothiazolin-3-one, 2-alkyl-4-isothiazolin-3-one, wherein the alkyl is selected from the group consisting of methyl, ethyl, butyl, propyl and mixtures thereof. The Examiner has noted that the examples are non-limiting as disclosed on page 52. Applicants note that the term "free of " is a positive recitation of Examples 14-26. Applicants would like to further point out that the examples are indeed intended to be non-limiting which allows for the presence or absence of components as exemplified. Applicants have provided examples wherein a Kathon CG

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component is present and wherein a Kathon CG component is absent. Thus, basis has been provided by the examples for Claim 52. Applicants kindly request reconsideration.

It is believed these changes do not involve any introduction of new matter. Consequently, entry of these changes is believed to be in order and is respectfully requested.

Upon entry of the amendments and new claims presented, Claims 1-54 remain in the application. Any additional claims fee due as a result of these amendments is charged to the Assignee's Deposit Account via the attached cover sheet.

### **INTERVIEW SUMMARY**

Applicants conducted a telephone interview with Examiner Neil Levy on September 26, 2003. In attendance for the Applicants was Ms. Linda M. Sivik. Applicants would like to thank Examiner Levy for the opportunity to speak with him. Examiner Levy provided an Interview Summary to the Applicants for the subject matter discussed.

### **Invention Synopsis**

The present invention relates to topical compositions for the treatment of microbial infections on the skin or scalp which include a polyvalent metal salt of pyrithione and include a metal ion source. The present invention also relates to methods of treating microbial infections of the skin or scalp using such compositions. The present invention further relates to methods of regulating or stimulating hair growth or inhibiting or reducing hair loss using such compositions.

### **Art Rejections**

#### **1) 35 U.S.C. § 102(e) as anticipated by, or in the alternative, § 103(a) as obvious over U.S. Patent 5,939,203 (Kappock et al)**

Claims 1-10, 13-22, 25-30, 36-38, 42-47, and 52-54 are rejected under 35 U.S.C. § 102(e) as being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Kappock et al (U.S. 5,939,203). Applicants respectfully traverse this rejection.

Kappock et al (U.S. 5,939,203) was disclosed as part a Supplemental Information Disclosure Statement filed by the Applicants on June 1, 2001. Kappock et al is directed toward an aqueous coating composition comprising water, a base medium being a resin, a pyrithione salt from .01% to 2% and zinc oxide from 0.001% to 10%. The Examiner has asserted that the instant

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ranges and ratios are seen as encompassing those of Kappock and as the preferred components are instantly claimed, the degree of precipitation would also be the same, although the Examiner states that 50% insoluble is not present in so many words.

However, Kappock et al is clearly directed toward towards coating compositions that are characterized by enhanced antimicrobial efficacy and resistance to discoloration, both in their wet state, and after drying, in the form of a dry film on a substrate. Clearly, Kappock et al is focused on films and further requires the use of a resin selected from the group consisting of vinyl, alkyd, epoxy, acrylic, polyurethane, polyester resins etc. The Examiner has stated that Kappock et al discloses well known antimicrobial additives useful in a myriad of applications – cosmetics, toiletries, and as an anti-dandruff agent in shampoos and hair products (col. 5, lines 40-43). Col. 5 lines 43-45 states that the aqueous compositions of the present invention are useful when formulated to contain the requisite components in addition to the antimicrobial component. A requisite component of Kappock et al is a resin. Clearly, the present invention is not directed toward the use of composition containing a resin.

In order to establish a prima facie cast of obviousness, the Examiner must show that (1) there is some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings, (2) there is a reasonable expectation of success, and (3) all of the limitations of the claims are taught or suggested in the prior art (M.P.E.P. § 2143).

The Examiner has not provided the requisite motivation to modify Kappock et al so as to obtain Applicants' invention. Unlike Applicants invention, Kappock et al does not recognize the problem for which the present invention has solved i.e., improved anti-dandruff efficacy can be dramatically increased in topical compositions by the use of polyvalent metal salts of pyrithione in combination with a metal ion source wherein the improved efficacy also allows for reduction of the levels of metal pyrithiones in anti-microbial compositions, thereby facilitating the production of safer products containing anti-microbials.

Further, Kappock et al is aimed at solving the problem of discoloration caused by extraneous species, by addition of metal ions. The present invention is aimed at enhancing antimicrobial efficacy. For discoloration to occur, extraneous color causing species (like iron) must be present in a formula. Kappock et al composition works in preventing discoloration, only when species that cause discoloration are present. In the present invention, the discoloration

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agents are irrelevant and the present invention can work in enhancing efficacy in all instances whether there is any discoloration agent present or not. Therefore, it is not obvious that Kappock et al prevention of discoloration has any relationship with antimicrobial efficacy. Likewise, with regarding to establishing in order a prima facie cast of obviousness, there is no motivation to modify Kappock et al so as to obtain Applicants' invention.

There is no description in any of the references regarding the relationship between the combination of these specific materials of the present invention with regard to anti-dandruff efficacy and the benefit of providing a solution to the problem for which the present invention has solved. Further, there is no motivation to look to Kappock et al and arrive at the unexpected benefit of the present invention. Applicants respectfully request reconsideration.

**2) 35 U.S.C. § 102(b) as anticipated by Korean Patent Application Number 10-1997-0010124 (Park)**

Claims 1-22, 25-28, 36-38, 47, 52, and 53 are rejected under 35 U.S.C. § 102(b) as being anticipated by Park (10-1997-0010124). Applicants respectfully traverse this rejection.

Park discloses a composition comprising zinc pyrithione to a zinc salt in a ratio from 50/1 to 1/6. In Table 1, Park discloses zinc pyrithione present in a composition at 0.5% and zinc salts at either 0.1 %, 0.5% and 1.5%. The Examiner states that Examples 8-14 shown insoluble (emulsified) forms of zinc pyrithione. The object of Park lies in that a zinc salt is added to the composition to solve the problem that ferrous ion contained in water or other components used for preparing the product easily combine with zinc pyrithione to form ferrous pyrithione of dark blue, which reduces the antibacterial activity and stability of the product and makes the appearance of the product poor.

In order to establish a prima facie cast of obviousness, the Examiner must show that (1) there is some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings, (2) there is a reasonable expectation of success, and (3) all of the limitations of the claims are taught or suggested in the prior art (M.P.E.P. § 2143).

The Examiner has not provided the requisite motivation to modify Park so as to obtain Applicants' invention. Unlike Applicants' invention, Park does not recognize the problem for

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which the present invention has solved i.e., improved anti-dandruff efficacy can be dramatically increased in topical compositions by the use of polyvalent metal salts of pyrithione in combination with a metal ion source wherein the improved efficacy also allows for reduction of the levels of metal pyrithiones in anti-microbial compositions, thereby facilitating the production of safer products containing anti-microbials.

Further, Park is aimed at solving the problem that ferrous ion contained in water or other components used for preparing the product easily combine with zinc pyrithione to form ferrous pyrithione of dark blue, which reduces the antibacterial activity and stability of the product and makes the appearance of the product poor. The present invention is aimed at enhancing antimicrobial efficacy. For discoloration to occur, extraneous color causing species (like iron) must be present in a formula. Park's composition works in preventing discoloration, only when species that cause discoloration are present. In the present invention, the discoloration agents are irrelevant and the present invention can work in enhancing efficacy in all instances whether there is any discoloration agent present or not. Therefore, it is not obvious that Park's prevention of discoloration has any relationship with antimicrobial efficacy. Likewise, with regard to establishing in order a prima facie cast of obviousness, there is no motivation to modify Park so as to obtain Applicants' invention.

There is no description in any of the references regarding the relationship between the combination of these specific materials of the present invention with regard to anti-dandruff efficacy and the benefit of providing a solution to the problem for which the present invention has solved. Further, there is no motivation to look to Park and arrive at the unexpected benefit of the present invention and a case of prima facie obviousness has not been met. Applicants respectfully request reconsideration.

**3) 35 U.S.C. § 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over U.S. 5,227,156 (Weise)**

Claims 1-30, 36-38, 42-46 and 53 are rejected under 35 U.S.C. § 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Wiese (U.S. 5,227,156). Applicants respectfully traverse this rejection.

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Wiese discloses that the activity of a thiazolinone preservative, in an anti-dandruff shampoo containing pyrithione, is maintained by adding a stabilizer comprising a zinc compound. Specifically, Wiese discloses an aqueous anti-dandruff shampoo comprising up to about 40% of a surfactant, from about 0.1% to about 2% zinc pyrithione, from about 1 to about 30 ppm of a preservative selected from the group consisting of 5-chloro-2alkyl-4-isothiazolin-3-one, 2-alkyl-4-isothiazolin-3-one, wherein the alkyl is selected from the group consisting of methyl, ethyl, butyl, propyl and mixtures thereof, from about 0.001% to about 1% of a preservative stabilizer comprising a zinc compound selected from the group consisting of a zinc salt of an organic acid, a zinc salt of an inorganic acid, zinc oxide, zinc hydroxide, and mixtures thereof, and the balance comprising water.

However, the present invention, as now claimed, is neither disclosed nor made obvious by Wiese. Weise only teaches and is limited to from about 0.001% to about 1% of a preservative stabilizer comprising a zinc compound. As stated above, Applicant's Examples 7, 16 and 20 all teach 1% of zinc sulfate and Examples 6, 12, 15, 19 discloses zinc sulfate present at 2%. Therefore, Applicants have submitted claims directed toward a metal ion source being present at greater than about 1% to about 10% in amended Claims 1, 10, 26, 28 and 36. In addition, Applicants have amended Claim 54 as a further independent claim directed toward a metal ion source being present from about 2% to about 10%, which is clearly allowable subject matter in view of Weise's limitation of from about 0.001% to about 1%.

Further, Weise is only directed toward compositions which require a specified thiazolinone preservative. Therefore, Applicants have submitted Claim 55 directed to a topical composition for treating microbes, in order to inhibit or prevent the growth on the skin or scalp of said microbes, consisting essentially of: from about 0.001% to about 10%, by weight of the composition, of an anti-microbial active selected from the group consisting of polyvalent metal salts of pyrithione; b) from about 0.001% to about 10%, by weight of the composition, of a metal ion source selected from group consisting of zinc salts, copper salts, silver salts, nickel salts, cadmium salts, mercury salts, bismuth salts, and mixtures thereof; and c) a topical carrier for the anti-microbial active and the metal salt; wherein the weight ratio of the metal source to the anti-microbial active is from about 5:100 to about 5:1 and wherein at least 50% of the anti-microbial active is insoluble in the composition.

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Further, Applicants have added new Claims 56 and 57. In Claim 56, component (a) of the claim consisting essentially of polyvalent metal salt(s) of pyrithione. In Claim 57, component (a) consists of polyvalent metal(s) of pyrithione. Both Claim 56 and 57 are allowable subject matter in view of Weise in that Weise discloses the isothiazolone preservative as being an anti-microbial active in the fourth full paragraph of Column 3.

Applicants' Claim 53 is directed toward a composition comprising from about 0.001% to about 10%, by weight of the composition, of an anti-microbial active selected from the group consisting of polyvalent metal salts of pyrithione; from about 0.5% to about 10%, by weight of the composition, of a metal ion source, and a topical carrier. Support for Claim 53 in the Applicants' specification can be found in Example 26 on page 63, wherein zinc sulfate is present at 0.5% and thus provides basis for the lower end of the metal ion source range above.

Applicants would like to direct the Examiner's attention to the point that, although Weiss claims a preservative stabilizer in the range of 0.001% to 1%. Weiss does not directionally teach a preservative stabilizer in the range of from about 0.5% to about 10%. Further, Wiese's examples teach away from the present invention. Wiese exemplifies very low levels of zinc oxide and zinc chloride in Example 1 and Example 2. Example 1 teaches 0.05 % by weight zinc chloride and Example 2 teaches 0.07% by weight of zinc oxide and 0.05% by weight of zinc chloride. Weise also teaches at Column 3, lines 47-49, that preferably the stabilizer is added at a level from about 0.01% to about 0.1%. Again, Weiss is clearly teaching in a direction away from the present invention. In the present invention, Examples 6, 7, 12, 15, 16, 19 and 20 disclose aqueous compositions comprising zinc sulfate present at 2% and 1%, respectively. Further, Example 26 of the present invention teaches a composition comprising zinc sulfate present at 0.5%. Clearly one of skill in the art would not be lead to the present invention by the teachings of Wiese. If one of skill in the art were to make the exemplified compositions of Wiese, they would not arrive at the present invention's compositions comprising an anti-microbial active selected from the group consisting of polyvalent metal salts of pyrithione; a metal ion source; and a topical carrier.

Therefore, as now amended, the present invention is novel and unobvious over Wiese, as supported by the remarks above.

### C nclusion

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Applicants have made an earnest effort to place their application in proper form and distinguish their claimed invention from the prior art which was applied in the April 11, 2003 Office Action. WHEREFORE, consideration of this application, consideration of the accompanying claims and claim amendments submitted herewith, withdrawal of the rejections under 35 U.S.C § 112 and 35 U.S.C § 102 and 35 U.S.C § 103, and allowance of Claims 1-55 are respectfully requested.

Respectfully submitted,  
David Francis Gavin et al.

By Linda M Sivik

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